

# **EXHIBIT A**

**酵 素**

**Enzyme for Biochemistry**

**Reagents**

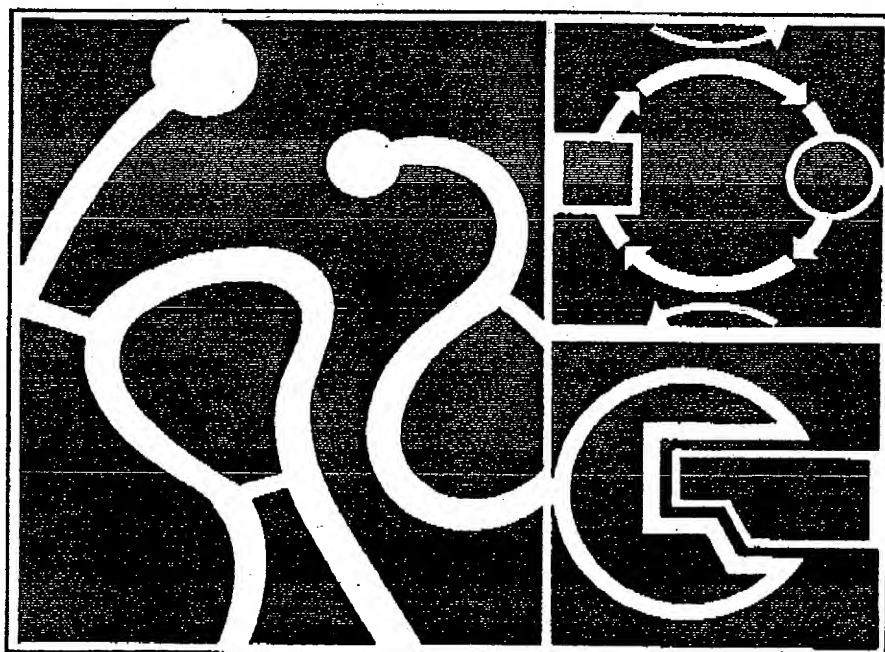
**MERCK**

**ENZYMES**  
**for**

**Biochemical research**

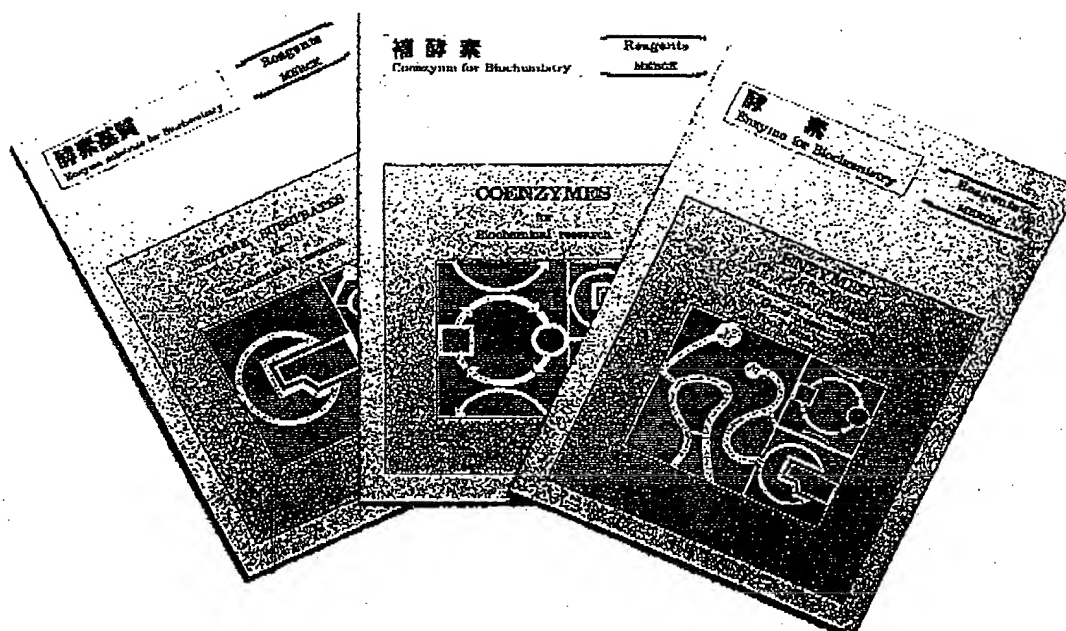
**Gene research**

**Food analysis**



1993年 9 月

**MERCK**



## 関東化学株式会社

### 試薬事業本部

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**24686 Ribonuclease A** (from bovine pancreas)

lyophilised

25 U/mg for biochemistry

EC 3.1.27.5

リボヌクレアーゼA (別名: RNase A)

**反応** リボ核酸を加水分解し、2', 3'-環状ピリミジンヌクレオチドを経由し、3'-ピリミジンヌクレオチドを生成

**起源** ウシ膵臓

**形状** 凍結乾燥品

**活性** 25 U/mg 以上 *no less than 25 U/mg*

**Test conditions**

1.4 ml Cytidine-2', 3'-cyclophosphate 22.2 mmol/l (resp. cytidine-2', 3'-cyclophosphate barium salt 11.1 mmol/l), dissolved in NaCl 0.1 mol/l (EDTA 0.1 mmol/l)

0.1 ml Ribonuclease (40 µg/ml), dissolved in NaCl 0.1 mol/l (EDTA 0.1 mmol/l)

Temperature: 25°C. Adjust to pH 7.1 and time 2 minutes. Titration of the liberated phosphoric acid groups with NaOH 0.01 mol/l by means of a pH-stat at pH 7.1.

1 U catalyses the formation of 1 µmole of phosphoric acid groups per minute under test conditions.

**共存酵素活性**

Deoxyribonuclease not detectable

**保存** 0°C - +6°C

**安定性** ディープフリーザー中で、-20°Cで乾燥保存した場合、12ヶ月以内に著しい活性の低下は認められない

**包装・価格** 100 mg 13,600

**7686 Saccharase** (from yeast)

lyophilised 300000 U/vial for biochemistry

EC 3.2.1.26

サッカラーゼ

(インベルターゼ, β-フルクトシダーゼ)

**系統名** β-D-Fructofuranoside fructohydrolase

**反応** スクロースなどのβ-D-フルクトフラノシドの非還元性のβ-D-フルクトフラノシド残基末端を加水分解

**起源** 酵母

**形状** 凍結乾燥品

**活性** 約 200 U/mg

**Test conditions**

8.9 ml Acetate buffer 0.1 mol/l, pH 4.5

1.0 ml Sucrose 1 mol/l, dissolved in redistilled water

0.1 ml Saccharase (1 mg/ml), dissolved in redistilled water

Incubate exactly 3 resp. 6 minutes at 25°C. To stop the reaction, add 0.2 ml of the reaction mixture to 2.0 ml Tris buffer 0.1 mol/l, dissolved in redistilled water.

For the determination of the liberated glucose, mix

2.0 ml Determination reagent (phosphate buffer 0.12 mol/l, pH 7.0; NaCl 0.15 mol/l; NAD 1.1 mmol/l; 5 U/ml glucose dehydrogenase; 0.1 U/ml mutarotase)

0.2 ml Reaction mixture (stopped with Tris buffer)

Temperature: 25°C. Measurement of ΔA at 366 nm at the end of the determination reaction (ca. 10-15 minutes) against blank.

Extinction coefficient (NADH):  $\epsilon_{366} = 3.4 \text{ cm}^2/\mu\text{mole}$ .

1 U catalyses the formation of 1 µmole of glucose per minute under test conditions.

**保存** 0°C - +6°C

**安定性** 4°Cで乾燥保存した場合、12ヶ月以内に著しい活性の低下は認められない

**包装・価格** 1 pack 16,400

# **EXHIBIT B**

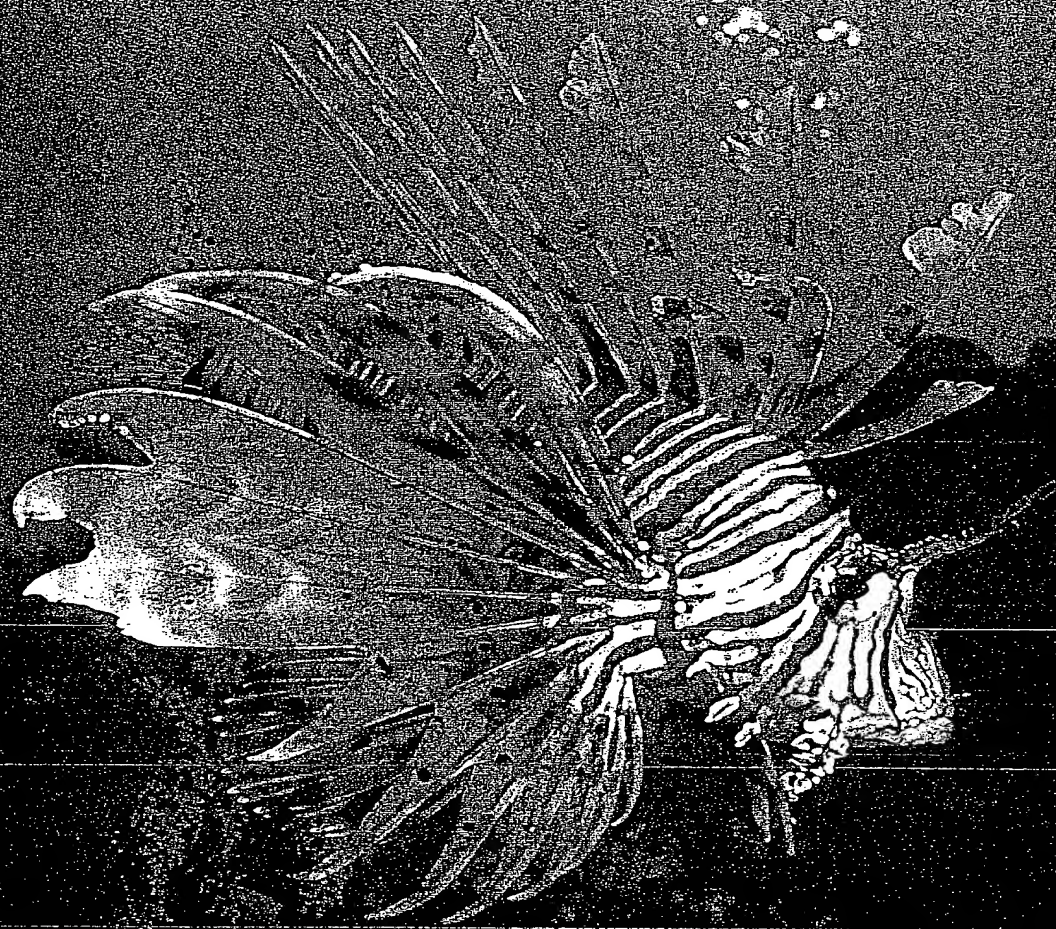
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**BOEHRINGER MANNHEIM**  
*Biochemica*

Biochemicals

Catalog 1996 '97

研究用試薬カタログ



## 切断とシーケンス用プロテアーゼ

Proteases for Cleavage and Sequencing

## プロテアーゼ

製 品 名	アプリケーション	特 異 性
トロンビン Thrombin 抽出源：ヒト血漿 凍結乾燥 緩衝剤で安定化、pH6.9 EC 3.4.21.5	血液凝固、医学研究。蛋白質構造研究及び生化学研究。	Argのカルボキシル基側でペプチド、エステル結合を特異的に切断するセリンエンドペプチダーゼ。
トリプシン Trypsin 抽出源：パン臓器 EC 3.4.21.4	蛋白質の分解と組織の分散。	塩基性アミノ酸ArgとLysのカルボキシル基側で蛋白質とペプチドを特異的に加水分解するセリンエンドペプチダーゼ。



切断とクェンス用プロテアーゼ  
Proteases for Cleavage and Sequencing  
プロテアーゼ

特 徴	阻 害 剤	製品番号	包装単位	希望価格
比活性：約120U/mg 酵素タンパク(Chromozym® THを基質として、25℃で測定)IU≒6.3NIH-unitsに相当 共存酵素活性：Factor Xa<3% 分子量：約 33.6kD 至適pH：8.2-9.0	DFP, TLCK, PMSF ベンザミジン, α <sub>1</sub> - アンチトリプシン, α <sub>2</sub> -マクログロブリン, アンチトロンピン, III-ヘパリン, ヒ ルジン, APMSF	602 400	20 U	¥10,000
形状：凍結乾燥、結晶化トリプシンより調製、塩類は含まない 比活性：約110U/mg凍結乾燥品(Chromozym® TRY <sup>+</sup> を基質として25℃で測定)≒約40U/mg凍結乾燥品(ベンゾイル-L-アルギニンエチルエステルを基質として25℃で測定) 分子量：23.5kD 至適pH：8.0	DFP, TLCK, PMSF ロイペプチン, 大豆 トリプシン, イソレ クター, 卵白トリプ シン, ヒトトリプ シン, α <sub>2</sub> -マクログロ ブリン, アンチトリ プシン, APMSF, ア ミン	109 819 109 827	500 mg 2 g	¥ 5,000 ¥17,400

about 110 U/mg freeze-dry product (measured at 25°C using Chromozym® TRY<sup>+</sup> as a substrate) ÷ about 40 U/mg freeze-dry product (measured at 25°C using benzoyl-L-arginine ethyl ester as a substrate)



# **EXHIBIT C**

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MP Biomedicals, LLC.  
Formerly ICN Biomedicals, Inc.

1263 S. Chillicothe Rd.  
Aurora, Ohio 44202

Telephone: 330/562-1500  
Toll Free: 800/854-0530  
Fax: 330/562-1987  
mailto:blotech@mpbio.com  
web: www.mpbio.com

A Member of the American Society For Quality

# ImmunO™

Nuclease(r)  
Catalog #: 32035  
Lot #: Typical

The *Staphylococcal* derived nuclease cleaves the 5'-phosphoryl ester bond of nucleic acids.

- Source:** *Staphylococcus aureus* gene expressed in recombinant *E. coli*
- Form:** Lyophilized in vials of 5 mg or 50 mg. The enzyme is also available in mega-unit quantities as a frozen liquid.
- Purity:** >99%, protein basis. Single band on SDS gradient gel electrophoresis on staining with Coomassie Blue R-250.
- Specific Activity:** 7,000 - 10,000 Units/mg (generally 8,000 Units/mg). One unit is equivalent to a change in  $A_{260}$  of 1.0 after 30 minutes at pH 8.8 and 37°C of a reaction mixture of acid soluble polynucleotides from native NDA. One  $\mu$ molar unit = 85  $A_{260}$  units.
- Properties:** The optimum pH for both RNase and DNase activity is between 9.0 and 10.0, and is dependent on the concentration of calcium ions. At high pH, less  $Ca^{2+}$  is required. The presence of  $Sr^{2+}$  results in high DNase activity and loss of RNase activity(1).
- Assay:** The assay of *Staphylococcus* nuclease is based on an increase in absorbance at 260 nm which accompanies the hydrolysis of nucleic acids<sup>(2)</sup>. This change has been found to correlate well with other changes reflecting DNA hydrolysis, such as an increase in viscosity, number of secondary phosphate groups which are liberated, and the production of acid soluble nucleotides<sup>(2)</sup>.
- Stability:** The enzyme is particularly stable; Stability extends to pH values as low as 0.1. At a concentration of 15 mg/ml there is no significant loss of activity after 20 minutes at 100°C.

Approved by: Joseph Dietz, Ph.D.  
Quality Control Director

Control #

# **EXHIBIT D**



Enzyme string search

## Search results

### Search-string [ribonuclease A]

3.-.-.- Hydrolases.  
 3.1.-.- Acting on ester bonds.  
 3.1.4.- Phosphoric diester hydrolases.  
 3.1.4.22 - Transferred entry: 3.1.27.5.

**PROTEIN NAME (2rsa):** Ribonuclease a  
**PROTEIN NAME (3rsa):** Ribonuclease a  
**PROTEIN NAME (4rsa):** Ribonuclease a (joint neutron and x-ray)

3.-.-.- Hydrolases.  
 3.1.-.- Acting on ester bonds.  
 3.1.26.- Endoribonucleases producing 5'-phosphomonoesters.  
 3.1.26.2 - Ribonuclease alpha.

**DESC:** Ribonuclease alpha.

3.-.-.- Hydrolases.  
 3.1.-.- Acting on ester bonds.  
 3.1.27.- Endoribonucleases producing other than 5'-phosphomonoesters.  
 3.1.27.5 - Pancreatic ribonuclease.

**PROTEIN NAME (1a2w):** Crystal structure of a 3d domain-swapped dimer of bovine pancreatic **ribonuclease a**  
**PROTEIN NAME (1a5p):** C[40,95]a variant of bovine pancreatic **ribonuclease a**  
**PROTEIN NAME (1a5q):** P93a variant of bovine pancreatic **ribonuclease a**  
**PROTEIN NAME (1afk):** Crystal structure of **ribonuclease a** in complex with 5'-diphosphoadenosine-3'-phosphate

**PROTEIN NAME (1afj):** Ribonuclease a in complex with 5'-diphosphoadenosine 2'-phosphate at 1.7 angstrom resolution  
 ... etc

3.-.-.- Hydrolases.  
 3.1.-.- Acting on ester bonds.  
 3.1.27.- Endoribonucleases producing other than 5'-phosphomonoesters.  
 3.1.27.10 - rRNA endonuclease.

**PROTEIN NAME (1de3):** Solution structure of the cytotoxic **ribonuclease alpha-sarcin**  
**PROTEIN NAME (1r4y):** Solution structure of the deletion mutant delta(7-22) of the cytotoxic **ribonuclease alpha-sarcin**

Number of entries matching your search string: 4

Total number of EC entries scanned: 4327



Enzyme string search

## Search results

**Search-string [ribonuclease T1]**

3.-.-.- *Hydrolases.*

3.1.-.- *Acting on ester bonds.*

3.1.27.- *Endoribonucleases producing other than 5'-phosphomonoesters.*

3.1.27.3 *Ribonuclease T(1).*

**OTHER NAME(S):** *Ribonuclease T1.*

**PROTEIN NAME (1bir):** *Ribonuclease t1, phe 100 to ala mutant complexed with 2' gmp*

**PROTEIN NAME (1bvi):** *Ribonuclease t1 (wildtype) complexed with 2'gmp*

**PROTEIN NAME (1det):** *Ribonuclease t1 carboxymethylated at glu 58 in complex with 2'gmp*

**PROTEIN NAME (1fys):** *Ribonuclease t1 v16c mutant*

*... etc*

*Number of entries matching your search string: 1*

*Total number of EC entries scanned: 4327*

Enzyme string search





Enzyme string search

## Search results

**Search-string [ribonuclease T2]**

*3.-.-.- Hydrolases.*

*3.1.-.- Acting on ester bonds.*

*3.1.27.- Endoribonucleases producing other than 5'-phosphomonoesters.*

*3.1.27.1 - Ribonuclease T(2).*

***OTHER NAME(S): Ribonuclease T2.***

*Number of entries matching your search string: 1*

*Total number of EC entries scanned: 4327*

Enzyme string search





Enzyme string search

## Search results

**Search-string [ribonuclease U2]**

*3.-.-.- Hydrolases.*

*3.1.-.- Acting on ester bonds.*

*3.1.27.- Endoribonucleases producing other than 5'-phosphomonoesters.*

*3.1.27.4 - Ribonuclease U(2).*

**OTHER NAME(S):** *Ribonuclease U2.*

**PROTEIN NAME (1rtu):** *Ustilago sphaerogena ribonuclease u2*

*Number of entries matching your search string: 1*

*Total number of EC entries scanned: 4327*

Enzyme string search







Enzyme string search

## Search results

### Search-string [phosphodiesterase I]

3.-.-.- Hydrolases.  
3.1.-.- Acting on ester bonds.  
3.1.4.- Phosphoric diester hydrolases.  
3.1.4.1 - Phosphodiesterase I.

#### *DESC: Phosphodiesterase I*

3.-.-.- Hydrolases.  
3.1.-.- Acting on ester bonds.  
3.1.4.- Phosphoric diester hydrolases.  
3.1.4.3 - Phospholipase C.

#### *OTHER NAME(S): Lipophosphodiesterase I.*

3.-.-.- Hydrolases.  
3.1.-.- Acting on ester bonds.  
3.1.4.- Phosphoric diester hydrolases.  
3.1.4.4 - Phospholipase D.

#### *OTHER NAME(S): Lipophosphodiesterase II.*

3.-.-.- Hydrolases.  
3.1.-.- Acting on ester bonds.  
3.1.4.- Phosphoric diester hydrolases.  
3.1.4.17 - 3',5'-cyclic-nucleotide phosphodiesterase.

**PROTEIN NAME (1ip2):** Molecular docking of competitive **phosphodiesterase** inhibitor, 4-[3-(cyclopentyloxy)-4-methoxyphenyl]-2-pyrrolidinone, rolipram

Number of entries matching your search string: **4**

Total number of EC entries scanned: **4327**

Enzyme string search





Enzyme string search

## Search results

### Search-string [nuclease P1]

3.-.-.- *Hydrolases.*

3.1.-.- *Acting on ester bonds.*

3.1.30.- *Endoribonucleases active with either ribo- or deoxyribonucleic*

3.1.30.1 *Aspergillus nuclease S(1).*

**COMMENTS:** *Penicillium citrinum nuclease P1.*

*Number of entries matching your search string: 1*

*Total number of EC entries scanned: 4327*

Enzyme string search





Enzyme string search

## Search results

### Search-string [nuclease S1]

3.-.-.- *Hydrolases.*

3.1.-.- *Acting on ester bonds.*

3.1.30.- *Endoribonucleases active with either ribo- or deoxyribonucleic*

3.1.30.1 *Aspergillus nuclease S(1).*

**OTHER NAME(S):** *Aspergillus nuclease S1.*

**OTHER NAME(S):** *Endonuclease S1.*

**OTHER NAME(S):** *Deoxyribonuclease S1.*

*Number of entries matching your search string: 1*

*Total number of EC entries scanned: 4327*

Enzyme string search



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